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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/131,385	08/07/98	STELLA	V 1257-0116P

LEONARD R. SVENSSON
BIRCH STEWART KOLASCH & BIRCH
P O BOX 747
FALLS CHURCH VA 22040-0747

HM12/0430

EXAMINER
AULAKH, C

ART UNIT	PAPER NUMBER
1612	

DATE MAILED:

04/30/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/131,385

Applicant(s)
Stella, V.J. et al.

Examiner
Charanjit Aulakh

Group Art Unit
1612



☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-18 is/are pending in the application.

Of the above, claim(s) 6, 7, and 13-15 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-5, 8-12, and 16-18 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☒ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1612

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, 8-12 and 16-18, drawn to compounds of formulas I and IV where R-O group represents Propofol, a process for preparing them, pharmaceutical compositions containing these compounds and a method of treatment using these compounds, classified in class 558, subclass 177+.

II. Claims 1-5, 8-12 and 16-18, drawn to compounds of formulas I and IV where R-O group represents pharmaceutical compounds other than Propofol, a process for preparing them, pharmaceutical compositions containing these compounds and a method of treatment using these compounds, classified in classes 546, 549 and 564, subclasses 42+, 218+ and 1+, respectively.

III. Claims 6, 7 and 13-15, drawn to compounds of formula III and a process for preparing them, classified in classes 546, 549, 564 and 568, subclasses 42+, 218+, 1+ and 18+, respectively.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I, II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions I through III are not disclosed as capable of use together. The inventions I and II are

Art Unit: 1612

directed to prodrugs of phosphate esters while Invention III is directed to totally different prodrugs. The different pharmaceutical compounds (representing R-O group) disclosed in Inventions I and II have different function, different mode of operation and different utility e.g ; Propofol is an anesthetic whereas camptothecin has utility in treating tumors or leukemia. Thus, there is no common core present which is essential to the utility. The Inventions I through III are structurally so divergent that a reference showing e.g ; compounds of invention I would not render compounds of invention II prima facie obvious. Search required for e.g ; compounds of invention I in class 558, subclass 177+ is not the same search for e.g ; compounds of invention II in classes 546, 549 and 564 and therefore, constitutes a burdensome search. Therefore, restriction requirement as indicated above is proper.

3. During a telephone conversation with Mr. Leonard R. Svensson on April 6, 1999, a provisional election was made with traverse to prosecute the invention of Group I (R-O group represents Propofol), claims 1-5, 8-12 and 16-18. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6, 7 and 13-15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-5, 8-12 and 16-18 have been examined to the extent that they read upon the elected Invention I. It is also of note that Inventions II and III may require further restriction.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

Art Unit: 1612

amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what is being treated. Propofol is an anesthetic agent and therefore, would have utility for producing anesthesia. The applicants are suggested to make an appropriate correction.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Cho (J. Pharm. Sci.) as well as by Varia (J. Pharm. Sci.).

Cho discloses Metronidazole Phosphate- - A water soluble prodrug for parenteral solutions of Metronidazole. The compound (metronidazole phosphate dipotassium salt) in scheme I on page 412 of this publication anticipates the instant claims.

Art Unit: 1612

Varia discloses Phenytoin prodrugs. The Compounds of formula IV on page 1087 of this publication anticipates the instant claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-5, 8-12 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (U.S. Patent no. 5,731,355) in view of Bundgaard (Design of Prodrugs).

Jones discloses pharmaceutical compositions of Propofol for producing anesthesia (see claim 1).

Jones does not disclose preparing phosphate esters of propofol (prodrugs). However,

Bundgaard teaches preparing esters as prodrugs for compounds containing hydroxyl groups such

as Trichloroethanol, Vidarabine and Metronidazole (see page 3, table 2). On page 8, second

paragraph, Bundgaard teaches that phosphate esters are one of the most commonly used esters

for increasing water solubility of alcoholic drugs. Therefore, it is the examiner's position that one

skilled in the art would have been motivated to modify the compounds and compositions of Jones

to prepare the instant phosphate esters of propofol since Propofol is an alcohol containing

pharmaceutical compound and Bundgaard teaches advantages of phosphate esters of alcoholic

Art Unit: 1612

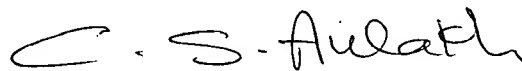
drugs as compared to the parent compounds such as enhanced water solubility, increased stability of solutions in vitro and their rapid enzymatic hydrolysis in vivo (see page 8, second paragraph).

10. The applicants did not provide EP 60491 reference and therefore, is not initialed on form 1449.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chana Aulakh whose telephone number is (703) 305-4482. The examiner can normally be reached on " Monday-Thursday " from 7:30 A.M. to 6:00 P.M.

If the attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. John Kight, can be reached on (703) 308-0204. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group's receptionist whose telephone number is (703) 308-1235.



CHARANJIT S. AULAKH

ASSISTANT EXAMINER